

**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

**Listing of Claims:**

1. (Currently amended) A method of screening a substance of interest for heme independent modulation of enzymatic activity of soluble guanylyl cyclase (sGC) comprising:

a) obtaining purified  $\alpha\beta^{Cys105}$  mutant soluble guanylyl cyclase enzyme or a cell lysate containing  $\alpha\beta^{Cys105}$  mutant soluble guanylyl cyclase enzyme;

b) assaying determining activity of said purified enzyme or cell lysate for formation of forming cGMP from GTP in a reaction medium in the presence of said substance;

c) assaying determining activity of said purified enzyme or cell lysate for formation of forming cGMP from GTP in a reaction medium in the absence of said substance;

optionally, d) carrying out steps b) and c) in the presence of an activator other than said substance;

e) comparing the results determinations from b) and c), and, d), if present, to yield a comparison result; and

f) assessing the ability activity of said substance to modulate cGMP production by said purified enzyme or cell lysate from the value of said comparison result, wherein increased or decreased formation of cGMP in the presence of said substance indicates that said substance is active for modulating heme independent cGMP production.

2. (Previously presented) The method of claim 1 wherein the outcome of step f) increased formation of cGMP in the presence of said substance indicates that said substance enhances cGMP production by said purified enzyme or cell lysate.

3-17. (Canceled)

18. (Currently amended) The method of claim 1 wherein the outcome of step f) decreased formation of cGMP in the presence of said substance indicates that said substance inhibits enhances cGMP production by said purified enzyme or cell lysate.

19. (Currently amended) The method of claim 18 wherein ~~the outcome of step f) said decreased formation of cGMP in the presence of said substance~~ indicates that said substance affects a structural element of the sGC enzyme other than a heme moiety to cause inhibition of sGC activity.

20. (Currently amended) The method of claim 2 wherein ~~the outcome of step f) increased formation of cGMP in the presence of said substance~~ indicates that said substance affects a structural element of the sGC enzyme other than a heme moiety to cause enhancement of sGC activity.

21. (Previously presented) The method of claim 1 wherein step d) is included and said activator comprises DTT.